Annals of Clinical and Analytical Medicine
Original Research

Exploring the role of Vitamin D in oral health and bone remodeling: Implications for apical periodontitis and tooth loss

Relationship between Vitamin D and apical periodontitis

Meltem Zihni Korkmaz[1], Banu Arıcıoğlu[2], Hatice Yemenoğlu[1], Özge Gören[2], Kaan Ilıcalı[2]
[1] Department of Periodontology
[2] Department of Endodontics, Faculty of Dentistry, Recep Tayyip Erdogan University, Rize, Turkey

Abstract
Aim: Vitamin D is a fat-soluble steroid hormone that has a pivotal role in Calcium, Phosphorus and bone mineralization. It plays a crucial biological role in maintaining normal bone health, growth, and development, including teeth and jaws. This retrospective study was designed to explore the correlation between Vitamin D levels and the prevalence of apical periodontitis, extracted teeth, the size of apical periodontitis
Material and Methods: A total of 114 patients were obtained from the archives of patients who were previously recorded at the Faculty of Dentistry for dental diagnosis. Patients were classified according to their Vitamin D levels. All teeth were evaluated as missing and apical periodontitis. The Kolmogorov-Smirnov test was used to evaluate the normality. Due to non-normal distribution, the relationship between diagnosis and Vitamin D level was examined using the Kruskal-Wallis test. A model was constructed with linear regression analysis.
Results: No significant difference was found between Vitamin D levels regarding the prevalence of extracted teeth, apical lesion. Apical lesion size and Vitamin D level were negatively correlated.
Discussion: In this study, it was considered that Vitamin D deficiency negatively affects the size of apical periodontitis. However, it does not affect the prevalence of tooth loss and apical periodontitis.

Keywords
Vitamin D, Apical Periodontitis, Tooth Loss

DOI: 10.4328/ACAM.21906 Received: 2023-08-25 Accepted: 2023-09-26 Published Online: 2023-10-07 Printed: 2023-10-15 Ann Clin Anal Med 2023;14(Suppl 3):S288-291
Corresponding Author: Meltem Zihni Korkmaz, Department of Periodontology, Faculty of Dentistry, Recep Tayyip Erdogan University, Rize, Turkey.
E-mail: meltem.zihni@erdogan.edu.tr P: +90 505 678 75 64
Corresponding Author ORCID ID: https://orcid.org/0000-0002-2574-0908
This study was approved by the Ethics Committee of Recep Tayyip Erdogan University (Date: 2023-05-11, No: 2023/116)

Introduction

Vitamin D is a fat-soluble steroid hormone obtained from exposure to sunlight, diet and dietary supplements. It has two forms: Vitamin D2 (ergocalciferol) and Vitamin D3 (cholecalciferol) and collaborates with two peptide hormones, calcitonin and parathyroid hormone, to uphold calcium homeostasis and bone turnover [1].

Vitamin D is converted into 25-hydroxivitamin D (25(OH)D) in the liver, which is the indicator for storage in the body. Then it is converted to the biologically active form in kidneys called 1.25 (OH)2D3, which plays a role in autocrine and paracrine functions, including cell proliferation, cell differentiation, and immune regulation [2].

Over the years, Vitamin D has gained recognition for its pivotal role in regulating calcium and phosphorus levels, as well as promoting bone mineralization [3]. It plays a crucial biological role in maintaining normal bone health, growth, and development, including teeth, by enhancing the absorption of calcium and phosphate in the small intestine [4]. Moreover, Vitamin D3 is instrumental in bone growth and remodeling through the activity of osteoblasts and osteoclasts. The biologically active form, 1.25 dihydroxy vitamin D (1.25(OH)2D3), not only fosters bone generation and maintenance, but also exhibits potent anti-inflammatory properties crucial for treatment prognosis [5]. Additionally, it serves as a robust immunomodulator, impacting innate and adaptive immune responses through interaction with the Vitamin D receptor in immune cells [6].

The classification for 1.25 dihydroxy Vitamin D levels is as follows: values less than 20 ng/ml indicate a deficiency, values between 20 and 30 ng/ml signify insufficiency and values of 30 ng/ml and above are considered sufficient [7]. Low levels of vitamin D have been linked to increased parathyroid hormone (PTH) secretion, escalated bone resorption, and conditions such as osteoporosis, osteomalacia, and heightened risk of fractures in the hip or other bones [8].

Apical periodontitis (AP) is a localized response occurring around the tooth's apex due to pulp necrosis or extensive periapical disease [9]. Metabolites from necrotic pulp prompt an inflammatory reaction in the periapical periodontal ligament and adjacent bone [10]. This response is histologically marked by an infiltration of lymphocytes and polymorphonuclear neutrophils, simulating bone resorption around the apex [11]. A study highlighted that vitamin D-resistant patients experience dental alterations and an increase in endodontic complications. Such patients often have dentitions vulnerable to bacterial invasion, leading to recurrent spontaneous pulp necrosis [12].

Multiple studies have indicated links between dental caries, delayed tooth eruption, periodontal diseases, alveolar bone quality, periodontal health, tooth loss, and Vitamin D levels. Moreover, a connection has been established between Vitamin D deficiency and delayed wound healing, gingival inflammation, tooth loss, and clinical attachment loss [13, 14]. Given its potent anti-proliferation, differentiation, and immunomodulatory effects, alongside its influence on alveolar bone metabolism and quality, Vitamin D level might impact the prevalence of apical periodontitis by engaging in anti-inflammatory activities in infected teeth and promoting jaw bone health [15]. Considering the effects of Vitamin D on inflammation reduction and alveolar bone formation, it is reasonable to speculate its potential role in infection control within periapical tissue. Thus, adequate Vitamin D levels could potentially contribute to resistance against the spread of endodontic diseases to the periapical region.

However, there is currently no published research examining the effects of Vitamin D on periapical lesion prevalence. Consequently, this retrospective cohort study was undertaken to explore the correlation between Vitamin D levels and the prevalence of apical periodontitis, extracted teeth, and root canal-treated teeth.

Material and Methods

This retrospective study was conducted in full accordance with the applicable ethical principles, including the World Medical Association Declaration of Helsinki of 1964 and later versions. The study protocol was approved by the Research Ethics Committee of Recep Tayyip Erdogan University; Date: Date: 2023-05-11, Number 2023/116.

A sample size calculation was performed using the software (GPower 3.1.0, Universitat Dusseldorf, Germany) to determine the number of individuals included in the study. According to the power analysis, a sample size of a total of 84 patients would give a medium-sized effect size (d=0.35) .

A total of 114 male/female patients with a median age of 34 years were obtained from the archives of patients who were previously recorded at the Faculty of Dentistry for dental diagnosis and treatment planning in the period from 2015 to 2022. Information about serum 1.25(OH)D levels in blood was obtained from medical history records. All panoramic radiographic images were obtained with the same device (Planmeca Promax 2D S2, Planmeca Oy; Helsinki, Finland) with the same exposure parameters (66 kVp, 8 mA, 16.6 s), according to the manufacturer's instructions and by adjusting the Frankfurt horizontal plane parallel to the ground and the vertical line to the sagittal plane.

The radiographs were evaluated simultaneously by two independent researchers with 10 and 20 years of experience. The calibration of observers was carried out on a set of 50 panoramic radiographs from a pilot phase of the Health 2000 Survey. All radiographs were evaluated under optimal conditions where the surrounding light could be controlled for the best possible radiographic contrast. The radiographs were placed in a viewing box and the light surrounding the radiograph was blocked. A 5-magnifying glass was used on most of the radiographs to enhance the image. In the cases of disagreement, a definitive evaluation was conducted by oral and maxillofacial radiologists.

The inclusion criteria were high-quality panoramic images that included all or part of the alveolar process of the maxilla and mandible. Images with satisfactory diagnostic quality (no artifact, or distortion, all trabecular and cortical structures are visible) were included. Patients with systemic disorders and bone metabolic diseases such as diabetes, osteoporosis, or hypo/hyperparathyroidism and using medication and smoking could affect the bone structure and bone mineralization, and inadequate diagnostic quality panoramic radiographs were excluded from the study. The images were randomly selected

with the aid of digital software (www. randomizer.org).
Patients were classified according to their Vitamin D levels [7];
Deficiency ≤ 20 ng/ml(n:71)
Insufficiency 20–30 ng/ml,(n:28)
Sufficiency >30 ng/ml (n:15)
All teeth were evaluated as missing and apical periodontitis. Multirooted teeth were classified according to the root exhibiting the most severe periapical condition. Criteria were as follows:
Apical periodontitis: Widening of the periodontal ligament (widening of the apical part of the periodontal ligament not exceeding two times the width of the lateral periodontal ligament space) or periapical radiolucency (radiolucency in connection with the apical part of the root, exceeding at least two times the width of the lateral part of the periodontal ligament.

Statistical Analysis

Jamovi software (version: 2.3.21) was used for the statistical analysis. Descriptive analysis was performed. The Kolmogorov-Smirnov test was used to evaluate the normality. Due to non-normal distribution, the relationship between diagnosis and Vitamin D level was examined using the Kruskal-Wallis test. A model was constructed with linear regression analysis. Significance was set at $p<0.05$.
The Kappa coefficient was calculated to test the compatibility between the observers. The agreement with the diagnoses for the presence of AP by tooth was 90% (Kappa 0.79).

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

A total of 114 individuals participated in the study, 61% (N=70) of whom were females. The median age of the participants was 34 years. While 62% (N=71) of the subjects had vitamin D level below 20, 13% (N=15) of them had vitamin D level between 30 and 100. The median Vitamin D level was 12 (Table 1).
No significant difference was found between Vitamin D levels regarding the prevalence of extracted teeth, apical lesion, ($p>0.05$) (Table 2).
The size of the lesion was the significant predictor for Vitamin D level ($p<0.001$) (Table 3) (Figure 1).

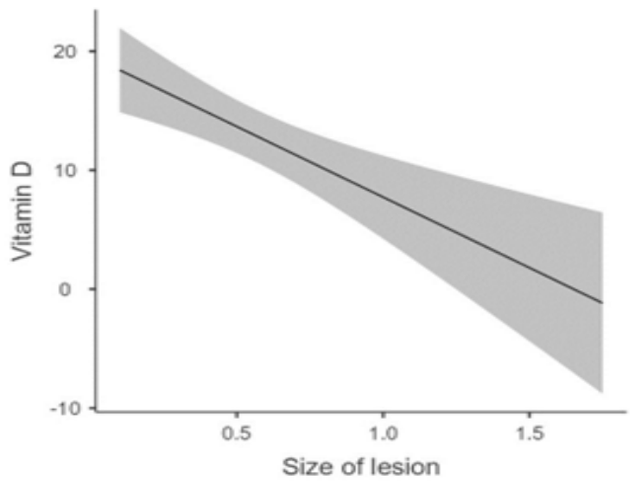

Figure 1. Size of Apical Lesion

Table 1. Demographic characteristics of participants.

Characteristic		N = 114
Gender	Female	70 (61%)
	Male	44 (39%)
Age		34 (27, 43)
Vitamin D level		
<20		71 (62%)
20-30		28 (25%)
30-100		15 (13%)
Vitamin D		12 (7, 24)

n (%); Median (IQR)

Table 2. Kruskal-Wallis test that examined the relationship between vitamin D levels and some diagnoses

Vitamin D level	<20		20-30		30-100		p value
	Mean	Median	Mean	Median	Mean	Median	
Apical lesion	0.41±0.5	0 (0-1)	0.54±0.51	1 (0-1)	0.38±0.5	0 (0-1)	0.454
Extracted teeth	1.66±1.76	1 (0-6)	1.64±1.64	1 (0-7)	2.29±1.61	3 (0-5)	0.303

Mean±Standard Deviation, Median (Min-Max)

Table 3. Linear regression analysis that established a model to predict Vitamin D levels based on lesion size

Predictor	Estimate	Stand. Estimate	SE	Lower (95% CI)	Upper (95% CI)	t	p
Intercept	19.6		2.01	15.56	23.64	9.73	<.001
Size of lesion	-11.87	-0.48	3.04	-17.98	-5.77	-3.9	<.001

Discussion

The optimal prognosis for endodontic treatment is dependent on the successful elimination of causative agents from the infected root canals. On the other hand, the immune response and biological mechanisms play a very important role in healing processes. Systemic factors such as chronic diseases, hormones, stress, and vitamin intake can alter the host's immune defense and as a consequence affect healing and success of dental treatment [16].
Vitamin D is an important hormone involved in the maintenance of serum calcium and phosphate levels, bone metabolism, and regulation of the inflammatory response [17].
Although there are many studies on the relationship between Vitamin D and dental disease, as far as we know there is no study investigating the prevalence of apical periodontitis in the literature. Vitamin D can influence alveolar bone formation and inflammatory reactions in periradicular tissues. The active form of vitamin D (1.25(OH)2D3) shows its effects by binding to the vitamin D receptor (VDR). Studies indicate that VDR and Vitamin D-dependent bone proteins are strongly expressed in the cells that play a role in alveolar bone formation. In the absence of a functional VDR, dental alveolar bone formation could be impaired. On the other hand, Vitamin D affects the onset and progression of inflammatory diseases by regulating the expression of several inflammatory cytokines [16]. In a study

by Ilan Rotstein and Joseph Katz, the prevalence of periapical abscess was investigated in patients with Vitamin D deficiency and they suggested that there may be a possible association between Vitamin D deficiency and the occurrence of periapical abscesses and the prevalence of periapical abscesses was higher in patients with Vitamin D deficiency [18]. In our study, no relationship was found between the prevalence of apical periodontitis and Vitamin D. This may be due to the limited number of the study population. However, the apical lesion size was significantly higher in the Vitamin D deficiency group. In the study by Restrepo et al., they stated that the periapical lesion size is one of the factors strongly affecting the treatment prognosis in apical periodontitis [19].

Studies including chronic periodontitis that show similar mechanisms with apical periodontitis are available in the literature. Antonoglou et al. designed a study in 2015 and investigated the relationship between chronic periodontitis and level of Vitamin D. According to this study, a significant association was found between serum 1,25(OH)2 D level and periodontal health status. In the group with low levels of Vitamin D, bone destruction was higher. Dietrich et al. also suggested in their study that both men and women have higher bone destruction in the vitamin D deficiency group [20]. Similarly to these studies, in our study, the apical lesion size was higher. This may be due to bone destruction because of poor mineralization and impaired immune response to microbial agents.

According to a study by Zhan et al. [21], it has been suggested that 25OHD was inversely associated with the incidence of tooth loss and each 10ug/L increase in serum 25OHD was associated with a 13% decreased risk of tooth loss. In another study by Jiminez et al. [22], the highest quintile predicted 25 OHD score was associated with a 14% lower risk of tooth loss compared with those in the lowest quintile. In contrast, in a study conducted by Pavlesen in 2016 [23], serum 25OHD was not associated with a 5-year incidence of tooth loss. Similarly, we did not find a relationship between tooth loss and vitamin D levels. More reliable results can be obtained with a larger sample size studies considering the reasons for tooth extraction.

Conclusion

In light of this study, it is considered that Vitamin D deficiency is a condition that negatively affects the prognosis of apical periodontitis as well as many other dental diseases due to its effects on bone metabolism and immune response. Recognizing the importance of Vitamin D may provide new perspectives on the protection of dental health and treatment of dental diseases.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Funding: *None*

Conflict of Interest

The authors declare that there is no conflict of interest.

References

1. Ross AC, Manson JE, Abrams SA, Aloia JF, Brannon PM, Clinton SK, et al. The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know. J Clin Endocrinol Metab. 2011;96(1):53-8.

2. Amano Y, Komiyama K, Makishima M. Vitamin D and periodontal disease. J Oral Sci. 2009; 51(1):11-20.

3. Tangpricha V, Koutkia P, Rieke SM, Chen TC, Perez A A, Holick M F. Fortification of orange juice with vitamin D: a novel approach for enhancing vitamin D nutritional health. Am J Clin Nutr. 2003; 77(6):1478-83.

4. Dusso AS, Brown AJ, Slatopolsky E. Vitamin D. Am J Physiol Renal Physiol. 2005;289(1): 8-28.

5. Yee Y.K., et al., Vitamin D receptor modulators for inflammation and cancer. Mini Rev Med Chem. 2005; 5(8):761-78.

6. Holick MF. Vitamin D deficiency. N Engl J Med. 2007; 357(3):266-81.

7. Holick MF. Vitamin D status: measurement, interpretation, and clinical application. Ann Epidemiol. 2009; 19(2):73-8.

8. Winzenberg TM, Powell S, Shaw KA, Jones G. Vitamin D supplementation for improving bone mineral density in children. Cochrane Database Syst Rev. 2010(10): Cd006944.

9. Meirinhos J, Martins JNR., Pereira B, Baruwa A, Gouveia J, Quaresma S A. Prevalence of apical periodontitis and its association with previous root canal treatment, root canal filling length and type of coronal restoration - a cross-sectional study. Int Endod J. 2020; 53(4):573-84.

10. Soares JA, Leonardo MR, Silva LAB, Filho MT, Ito IY. Histomicrobiologic aspects of the root canal system and periapical lesions in dogs' teeth after rotary instrumentation and intracanal dressing with Ca(OH)2 pastes. J Appl Oral Sci. 2006; 14(5):355-64.

11. Liapatas S, Nakou M, Rontogianni D. Inflammatory infiltrate of chronic periradicular lesions: an immunohistochemical study. Int Endod J. 2003; 36(7):464-71.

12. Souza AP, Kobayashi TY, Neto NL, Silva S L B, Machado MAAM, Oliveira TM. Dental manifestations of patient with vitamin D-resistant rickets. J Appl Oral Sci. 2013;21(6):601-6.

13. Schroth R J, Levi J A, Sellers E A, Friel J, Kliewer E, Moffatt M E K. Vitamin D status of children with severe early childhood caries: a case-control study. BMC Pediatr. 2013;13:174.

14. Hujoel PP. Vitamin D and dental caries in controlled clinical trials: systematic review and meta-analysis. Nutr Rev. 2013; 71(2):88-97.

15. Krall EA, Wehler C, Garcia RI, Harris SS, Dawson-Hughes B. Calcium and vitamin D supplements reduce tooth loss in the elderly. Am J Med. 2001; 111(6):452-6.

16. Holland R, Filho JEG, Cintra L T A, Queiroz IOA, Estrela C. Factors affecting the periapical healing process of endodontically treated teeth. J Appl Oral Sci. 2017;25(5):465-76.

17. Zittermann A. Vitamin D in preventive medicine: are we ignoring the evidence Br J Nutr. 2003;89(5):552-72.

18. Rotstein I. Katz J. Prevalence of periapical abscesses in vitamin D deficient patients. Am J Dent. 2021;34(3):163-5.

19. Restrepo-Restrepo FA, Cañas-Jiménez SJ, Romero-Albarracín RD, Villa-Machado P A, Pérez-Cano M I, Tobón-Arroyave SI. Prognosis of root canal treatment in teeth with preoperative apical periodontitis: a study with cone-beam computed tomography and digital periapical radiography. Int Endod J. 2019; 52(11):1533-46.

20. Dietrich T, Joshipura KJ, Dawson-Hughes B, Bischoff-Ferrari HA. Association between serum concentrations of 25-hydroxyvitamin D3 and periodontal disease in the US population. Am J Clin Nutr. 2004;80(1):108-13.

21. Zhan Y, Samietz S, Holtfreter B, Hannemann A, Meisel P, Nauck M, et al. Prospective Study of Serum 25-hydroxy Vitamin D and Tooth Loss. J Dent Res. 2014; 93(7):639-44.

22. Jimenez M, Giovannucci E, Kaye E K, Joshipura K J, Dietrich T. Predicted vitamin D status and incidence of tooth loss and periodontitis. Public Health Nutr. 2014; 17(4):844-52.

23. Pavlesen S, Mai X, Wactawski-Wende J, LaMonteM J, Hovey K M, Genco R J. Vitamin D Status and Tooth Loss in Postmenopausal Females: The Buffalo Osteoporosis and Periodontal Disease (OsteoPerio) Study. J Periodontol. 2016; 87(8):852-63.

How to cite this article:

Meltem Zihni Korkmaz, Hatice Yemenoğlu, Banu Arıcıoğlu, Özge Gören, Kaan Ilıcalı. *Exploring the role of Vitamin D in oral health and bone remodeling: Implications for apical periodontitis and tooth loss. Ann Clin Anal Med 2023;14(Suppl 3):S288-291*

This study was approved by the Ethics Committee of Recep Tayyip Erdogan University (Date: 2023-05-11, No: 2023/116)